

WE CLAIM:

1. An isolated presenilin associated membrane protein (PAMP), or a functional fragment thereof.
2. The PAMP of claim 1, which is human PAMP (SEQ ID NO: 14).
3. The PAMP of claim 1, which is mouse PAMP (SEQ ID NO: 16) *D. melanogaster* (SEQ ID NO: 18), or *C. elegans* PAMP (SEQ ID NO: 12).
4. The PAMP of claim 1, which is a mutant PAMP.
5. The mutant PAMP of claim 4 wherein the mutation results in biochemical changes similar to those included by mutations in presenilin-1, presenilin-2, or β -amyloid precursor protein associated with familial Alzheimer's Disease.
6. The mutant PAMP of claim 5, wherein the mutation is to an amino acid residue selected from the group consisting of D336, Y337, C230, and both D336 and Y337.
7. A transgenic animal, comprising a transgene encoding presenilin associated membrane protein (PAMP) which is expressed in neural cells such that the animal detectably expresses *PAMP* mRNA.
8. The transgenic animal of claim 7, which detectably expresses PAMP protein.
9. The transgenic animal of claim 8, which processes β -amyloid precursor protein to produce amyloid- β peptide.
10. The transgenic animal of claim 7, which is a mouse.

11. The transgenic animal of claim 7, wherein PAMP is human PAMP (SEQ ID NO: 14).
12. The transgenic animal of claim 17, wherein said PAMP is a mutant PAMP.
13. The transgenic animal of claim 7, further comprising a second transgene encoding a human presenilin-1, human presenilin-2 or human β -amyloid precursor protein, wherein the human presenilin-1, human presenilin-2, or human β -amyloid precursor protein is expressed at a level that permits its detection.
14. An animal containing a nucleic acid that expresses an endogenous presenilin associated membrane protein (PAMP) at a higher or lower level relative to expression level in a wild-type animal.
15. The animal of claim 14, prepared by homologous recombination mediated targeting of an endogenous PAMP gene.
16. The animal of claim 14, prepared by translocation of P-elements.
17. The animal of claim 14, prepared by chemical mutagenesis.
18. The cell of claim 14, wherein the mutation results in biochemical changes similar to those induced by mutations in presenilin-1, presenilin-2 or β -amyloid precursor protein associated with familial Alzheimer's Disease.
19. A reconstituted system for measuring presenilin associated membrane protein (PAMP) activity, comprising PAMP or a functional fragment thereof, and a PAMP substrate.
20. The reconstituted system of claim 19, which is a whole cell.

21. The reconstituted system of claim 19, wherein said whole cell contains a first nucleic acid that expresses said PAMP and a second nucleic acid that expresses said substrate.

22. The reconstituted system of claim 19, wherein said substrate is selected from the group consisting of presenilin-1 protein, presenilin-2 protein and β -amyloid precursor protein.

23. A complex between a presenilin associated membrane protein (PAMP) and an agent which provides a detectable conformational change in said PAMP upon interaction with a substance being analyzed for activity against a neurodegenerative disease.

24. The complex of claim 23, further comprising presenilin 1 protein, presenilin 2 protein, β -amyloid precursor protein, or a combination thereof.

25. A method for detecting a mutation in presenilin associated membrane protein (PAMP) associated with disease or a related neurological disorder, which method comprises detecting a variation in a sequence of a gene encoding PAMP obtained from an individual diagnosed with or suspected of having a neurodegenerative disorder.

26. A method for diagnosing individuals predisposed to or having a neurodegenerative disorder, which method comprises detecting a mutation in a gene encoding PAMP obtained from an individual.

27. The method according to claim 26, wherein detection of the mutation comprises measuring a level of transcriptional activity of the gene.

28. The method according to claim 26, wherein detection of the mutation comprises measuring PAMP activity.

29. The method of claim 28, wherein said PAMP activity comprises PAMP expression level or activity of a product of a PAMP modified substrate.

30. A method for identifying a compound that modulates PAMP activity, which method comprises detecting modulation of PAMP expression in a transgenic animal that expresses PAMP, wherein the animal is contacted with the compound.

31. A method for identifying a compound that modulates PAMP activity, which method comprises detecting a change in PAMP activity in the reconstituted system of claim 19 contacted with a test compound.

32. A method for identifying a compound that modulates PAMP activity, which method comprises detecting a conformational or functional change in PAMP in the complex of claim 23 contacted with a test compound.

33. The method of claim 32, wherein the compound is a protein that interacts with PAMP.